PATENT ZFW



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 03-465-D (400/151))

mtha Application of:)
)
McSwiggen et al.)
) Examiner: TBD
Serial No.: 10/826,966)
) Group Art Unit: TBD
Filing Date: April 16, 2004)
) Confirmation No. 2134
For: RNA Interference Mediated Inhibition of	Ì

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Sir:

TRANSMITTAL LETTER

In regard to the above identified application:

Gene Expression Using Chemically Modified Short Interfering Nucleic Acid

- 1. We are transmitting herewith the attached papers for the above identified new patent application:
 - Information Disclosure Statement;
 Information Disclosure Statement (IDS) PTO-1449 Form; and
 Return Receipt Postcard.
- 2. With respect to additional fees, no additional fee is required.
- 3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
- 4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450 on August 10 2004.

Rv ·

Michael S. Greenfiel

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 03-465-D (400/151))

In the	Application of:	. }	
	McSwiggen et al.)	
)	Examiner: TBD
Seria	l No.: 10/826,966)	
)	Group Art Unit: TBD
Filing	Date: April 16, 2004)	
)	Confirmation No. 2134
For:	RNA Interference Mediated Inhibition of)	
	Gene Expression Using Chemically)	
	Modified Short Interfering Nucleic Acid)	

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. This application is a continuation-in-part of US Serial No. 10/757,803 filed January 14, 2004, which is a continuation-in-part of US Serial No. 10/720,448 filed November 24, 2003, which is a continuation-in-part of US Serial No. 10/693,059 filed October 23, 2003, which is a continuation-in-part of US Serial No. 10/444,853 filed May 23, 2003, which is a continuation-in-part of US Serial No. 10/444,853 filed May 23, 2003, which is a continuation-in-part of US Serial No. 10/417,012 filed April 16, 2003 and is relied upon for an earlier filing date under 35 U.S.C. § 120. In accordance with Rule 37 CFR §1.98(d), all references have been previously cited and submitted to the Patent and Trademark Office with the prior application US Serial No. 10/444,853.

The Office has waived the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent

applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC § 371 after June 30, 2003. In accordance with this waiver, cited U.S. patents and U.S. patent application publications are not enclosed.

This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief is in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned attorney by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

U. S. PATENT APPLICATION DOCUMENTS

- * Blatt et al., U.S. Patent Application No. 09/740,332 filed December 18, 2000
- * Matulic-Adamic et al., U.S. Patent Application No. 10/151,116 filed May 17, 2002
- * Vargeese et al., U.S. Patent Application No. 10/201,394 filed August 13, 2001
- * McSwiggen et al., U.S. Patent Application No. 10/417,012 filed April 16, 2003
- * McSwiggen et al., U.S. Patent Application No. 10/422,704 filed April 24, 2003
- * Vargeese et al., U.S. Patent Application No. 10/427,160 filed April 30, 2003
- * McSwiggen et al., U.S. Patent Application No. 10/444,853 filed May 23, 2003
- * McSwiggen et al., U.S. Patent Application No. 10/652,791 filed August 29, 2003
- * McSwiggen et al., U.S. Patent Application No. 10/693,059 filed October 23, 2003
- * McSwiggen et al., U.S. Patent Application No. 10/720,448 filed November 24, 2003
- * Vaish et al., U.S. Patent Application No. 10/727,780 filed December 3, 2003
- * Thompson et al., U.S. Patent Application No. 60/082,404 filed April 20, 1998
- * Beigelman et al., U.S. Patent Application No. 60/358,580 filed February 20, 2002
- * Matulic-Adamic et al., U.S. Patent Application No. 60/362,016 filed March 6, 2002

- * Beigelman et al., U.S. Patent Application No. 60/363,124 filed March 11, 2002
- * Beigelman et al., U.S. Patent Application No. 60/386,782 filed June 6, 2002
- * Usman et al., U.S. Patent Application No. 60/402,996 filed August 13, 2002
- * Beigelman et al., U.S. Patent Application No. 60/406,784 filed August 29, 2002
- * Beigelman et al., U.S. Patent Application No. 60/408,378 filed September 5, 2002
- * Beigelman et al., U.S. Patent Application No. 60/409,293 filed September 9, 2002
- * Beigelman et al., U.S. Patent Application No. 60/440,129 filed January 15, 2003
- * Jadhati et al., U.S. Patent Application No. 60/543,480 filed February 10, 2004
- * Hoffman et al., U.S. Patent Publication No. 2001/0007666 published July 12, 2001
- * Caster, U.S. Patent Publication No. 2002/0130430 published September 19, 2002

U.S. PATENTS

- * Cook et al., U.S. Patent No. 5,138,045 published August 11, 1992
- * Lin et al., U.S. Patent No. 5,214,136 published May 25, 1993
- * Sproat, U.S. Patent No. 5,334,711 published August 2, 1994
- * Usman et al., U.S. Patent No. 5,627,053 published May 6, 1997
- * Usman et al., U.S. Patent No. 5,631,360 published May 20, 1997
- * Cook et al., U.S. Patent No. 5,670,633 published September 23, 1997
- * Eckstein et al., U.S. Patent No. 5,672,695 published September 30, 1997
- * Beigelman et al., U.S. Patent No. 5,716,824 published February 10, 1998
- * Buhr et al., U.S. Patent No. 5,792,847 published August 11, 1998
- * Usman et al., U.S. Patent No. 5,804,683 published September 8, 1998
- * Robinson et al., U.S. Patent No. 5,814,620 filed September 29, 1998

- * Usman et al., U.S. Patent No. 5,831,071 published November 3, 1998
- * Sullenger et al., U.S. Patent No. 5,854,038 filed December 29, 1998
- * Scaringe et al., U.S. Patent No. 5,889,136 published March 30, 1999
- * Crooke, U.S. Patent No. 5,898,031 published April 27, 1999
- * Adamic et al., U.S. Patent No. 5,998,203 published December 7, 1999
- * Brennan, U.S. Patent No. 6,001,311 published December 14, 1999
- * Cook et al., U.S. Patent No. 6,005,087 published December 21, 1999
- * Scaringe et al., U.S. Patent No. 6,008,400 published December 28, 1999
- * Bellon et al., U.S. Patent No. 6,054,576 published April 25, 2000
- * Crooke, U.S. Patent No. 6,107,094 published August 22, 2000
- * Scaringe et al., U.S. Patent No. 6,111,086 published August 29, 2000
- * Usman et al., U.S. Patent No. 6,117,657 published September 12, 2000
- * Manoharan et al., U.S. Patent No. 6,153,737 published November 28, 2000
- * Bellon et al., U.S. Patent No. 6,162,909 published December 19, 2000
- * Kaplitt et al., U.S. Patent No. 6,180,613 published January 30, 2001
- * Wang et al., U.S. Patent No. 6,235,310 published May 22, 2001
- * Manoharan et al., U.S. Patent No. 6,235,886 published May 22, 2001
- * Adamic et al., U.S. Patent No. 6,248,878 published June 19, 2001
- * Gold, U.S. Patent No. 6,300,074 published October 9, 2001
- * Bellon et al., U.S. Patent No. 6,303,773 published October 16, 2001
- * Guzaev et al., U.S. Patent No. 6,335,434 published January 1, 2002
- * Usman et al., U.S. Patent No. 6,353,098 published March 5, 2002
- * Usman et al., U.S. Patent No. 6,362,323 published March 26, 2002

- * Beigelman et al., U.S. Patent No. 6,395,713 published May 28, 2002
- * Usman et al., U.S. Patent No. 6,437,117 published August 20, 2002
- * Vook et al., U.S. Patent No. 6,447,796 published September 10, 2002
- * Usman et al., U.S. Patent No. 6,469,158 published October 22, 2002
- * Buhr et al., U.S. Patent No. 6,476,205 published November 5, 2002
- * Fire et al., U.S. Patent No. 6,506,559 published June 14, 2003
- * Cook et al., U.S. Patent No. 6,528,631 published March 4, 2003
- * Sagara, U.S. Patent No. 6,586,524 published July 1, 2003
- * Doucette-Stamm et al., U.S. Patent No. 6,617,156 published September 9, 2003

FOREIGN PATENT DOCUMENTS

- * Graham et al., Australian Patent No. 20001240375 (Old Application No. 4037501) dated March 16, 2001
- * Kreutzer et al., Canadian Patent No, 2,359,180 published August 3, 2002
- Kreutzer et al., European Patent No. 1144623 published January 29, 2002
- * Arnold et al., International Publication No. WO 89/02439 published March 23, 1989
- * Gillespie et al., International Publication No. WO 90/14090 published November 29, 1990
- * Rossi et al., International Publication No. WO 91/03162 published March 21, 1991
- * Eckstein et al., International Publication No. WO 92/07065 published April 30, 1992
- * Usman et al., International Publication No. WO 93/15187 published August 5, 1993
- * Draper et al., International Publication No. WO 93/23569 published November 25, 1993
- * Agrawal et al., International Publication No. WO 94/01550 published January 20, 1994
- * Sullivan et al., International Publication No. WO 94/02595 published February 3, 1994
- * Usman et al., International Publication No. WO 95/06731 published March 9, 1995

- * Dudycz et al., International Publication No. WO 95/11910 published May 4, 1995
- * Ansell et al., International Publication No. WO 96/10390 published April 11, 1996
- * Choi et al., International Publication No. WO 96/10391 published April 11, 1996
- * Holland et al., International Publication No. WO 96/10392 published April 11, 1996
- * Beigelman et al., International Publication No. WO 97/26270 published July 24, 1997
- * Woolf et al., International Publication No. WO 98/13526 published April 2, 1998
- Klimuk, International Publication No. WO 99/04819 published February 4, 1999
- * Beigelman et al., International Publication No. WO 99/05094 published February 4, 1999
- * Deschamps de Paillette et al., International Publication No. WO 99/07409 published February 18, 1999
- * Wengel et al., International Publication No. WO 99/14226 published March 25, 1999
- * Barry et al., International Publication No. WO 99/31262 published June 24, 1999
- * Fire et al., International Publication No. WO 99/32619 published July 1, 1999
- * Graham et al., International Publication No. WO 99/49029 published September 30, 1999
- Waterhouse et al., International Publication No. WO 99/53050 published October 21, 1999
- Thompson et al., International Publication No. WO 99/54459 published October 28, 1999
- * Heifetz et al., International Publication No. WO 99/61631 published December 2, 1999
- Plaetinck et al., International Publication No. WO 00/01846 published January 13, 2000
- * Gurney et al., International Publication No. 00/17369 published March 30, 2000
- * Kreutzer et al., International Publication No. WO 00/44895 published August 3, 2000
- * Li et al., International Publication No. WO 00/44914 published August 3, 2000
- * Sheen, International Publication No. WO 00/49035 published August 24, 2000

- * O'Hare and Normand, International Publication No. WO 00/53722 published September 14, 2000
- * Pachuk et al., International Publication No. WO 00/63364 published October 26, 2000
- * Wengel et al., International Publication No. WO 00/66604 published November 9, 2000
- * Satishchandran et al., International Publication No. WO 01/04313 published January 18, 2001
- * Mello et al., International Publication No. WO 01/29058 published April 26, 2001
- * Zernicka-Goetz et al., International Publication No. WO 01/36646 published May 25, 2001
- * Grossniklaus, International Publication No. WO 01/38551 published May 31, 2001
- Churikov et al., International Publication No. WO 01/42443 published June 14, 2001
- * Driscoll et al., International Publication No. WO 01/49844 published July 12, 2001
- * Cogoni et al., International Publication No. WO 01/53475 published July 26, 2001
- Beach et al., International Publication No. WO 01/68836 published September 20, 2001
- * Honer et al., International Publication No. WO 01/70944 published September 27, 2001
- * Graham et al., International Publication No. WO 01/70949 published September 27, 2001
- Deak et al., International Publication No. WO 01/72774 published October 4, 2001
- * Tuschl et al., International Publication No. WO 01/75164 published October 11, 2001
- * Arndt et al., International Publication No. WO 01/92513 published December 6, 2001
- * Mushegian et al., International Publication No. WO 01/96584 published December 20, 2001
- * Beigelman et al., International Publication No. WO 02/22636 published February 28, 2002
- * Bennett et al., International Publication No. WO 02/22636 published March 21, 2002
- * Echeverri et al., International Publication No. WO 02/38805 published May 16, 2002
- * Tuschl et al., International Publication No. WO 02/44321 published June 6, 2002

- Kreutzer et al., International Publication No. WO 02/55692 published July 18, 2002
- * Kreutzer et al., International Publication No. WO 02/55693 published July 18, 2002
- * Beigelman et al., International Publication No. WO 02/094185 (PCT/US02/15876) published November 28, 2002
- * Ahlheim et al., International Publication No. WO 03/024420 published March 27, 2003
- * Wang et al., International Publication No. WO 03/046185 published June 5, 2003
- * Wang et al., International Publication No. WO 03/047518 published June 12, 2003
- * Woolf et al., International Publication No. WO 03/064625 published August 7, 2003
- * Woolf et al., International Publication No. WO 03/064626 published August 7, 2003
- * McSwiggen et al., International Publication No. WO 03/070918 (PCT/US03/05346) published August 28, 2003
- * McSwiggen et al., International Publication No. WO 03/074654 (PCT/US03/05028) published September 12, 2003
- * Davidson et al., International Publication No. WO 04/013280 published February 12, 2004

OTHER DOCUMENTS

- * Adah et al., "Chemistry and Biochemistry of 2',5'-Oligoadenylate-Based Antisense Strategy," *Current Medicinal Chemistry*, 8, 1189-1212 (2001)
- * Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," <u>Trends Cell Biol.</u> 2:139-144 (1992)
- * Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a *retro-inverso* delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," Nucleic Acids Research 26:4910-4916 (1998)
- * Allshire, "RNAi and Heterochromatin A Hushed-up Affair," <u>Science</u> 297:1818-1819 (2002)

- * Andrews and Faller, "A rapid micropreparation technique for extraction of DNAbinding proteins from limiting numbers of mammalian cells," *Nucleic Acids Research* 19:2499 (1991)
- * Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," Cell 22:611-620 (1980)
- * Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent α1(I) Collagen by a Homologous Transcriptionally Self-Silenced Transgene," Molecular and Cellular Biology, 274-283 (1999)
- * Bannai et al., "Effect of Injection of Antisense of Oligodeoxynucleotides of GAD Isozymes into Rat Ventromedial Hypothalamus on Food Intake and Locomotor Activity," Brain Research 784:305-315 (1998)
- * Bannai et al., "Water-absorbent Polymer as a Carrier for a Discrete Deposit of Antisense Oligodeoxynucleotides in the Central Nervous System," <u>Brain Research Protocols</u> 3:83-87 (1998)
- * Bartel and Szostak, "Isolation of New Ribozymes from a Large Pool of Random Sequences," <u>Science</u> 261:1411-1418 (1993)
- * Basi et al., "Antagonistic Effects of β -Site Amyloid Precursor Prtein-cleaving Enzymes 1 and 2 on β -Amyloid Peptide Production in Cells*," *The Journal of Biological Chemistry*, 278, 31512-31520 (2003)
- * Bass, "Double-Stranded RNA as a Template for Gene Silencing," *Cell*, 101, 235-238 (2000)
- * Bass, "The short answer," *Nature* 411:428-429 (2001)
- * Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," <u>Tetrahedron</u> 49:1925-1963 (1993)
- * Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," <u>Science</u> 257:635-641 (1992)
- * Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," <u>The Journal of Biological Chemistry</u> 270:25702-25708 (1995)
- * Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," *Nucleosides & Nucleotides* 16:951-954 (1997)

- * Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," <u>Bioconjugate Chem.</u> 8:204-212 (1997)
- * Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," Nature 409:363-366 (2001)
- * Bettinger et al., "Size Reduction of Galactosylated PEI/DNA Complexes Improves Lectin-Mediated Gene Transfer into Hepatocytes," *Bioconjugate Chem.*, 10, 558-561 (1999)
- * Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," *Journal of Pharmaceutical Sciences* 87:1308-1315 (1998)
- * Boado, "Antisense drug delivery through the blood-brain barrier," *Advanced Drug Delivery Reviews* 15:73-107 (1995)
- * Bongartz et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," *Nucleic Acids Research* 22:4681-4688 (1994)
- * Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus iterative selection methods," <u>TIBTECH</u> 12:268-275 (1994)
- * Breaker, "Are engineered proteins getting competition from RNA?" <u>Current</u> Opinion in Biotechnology 7:442-448 (1996)
- * Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," *Biotechnology and Bioengineering (Combinatorial Chemistry)* 61:33-45 (1998)
- * Broaddus et al., "Distribution and stability of antisense phosphorothioate oligonucleotides in rodent brain following direct intraparenchymal controlled-rate infusion," Neurosurg. Focus 3(5):Article 4 (1997)
- * Broaddus et al., "Distribution and stability of antisense phosphorothioate oligonucleotides in rodent brain following direct intraparenchymal controlled-rate infusion," <u>J Neurosurg</u> 88:734-742 (1998)
- * Brody and Gold, "Aptamers as therapeutic and diagnostic agents," Reviews in Molecular Biotechnology 74:5-13 (2000)
- * Buckwold et al., "Effects of a Naturally Occurring Mutation in the Hepatitis B Virus Basal Core Promoter on Precore Cene Expression and Viral Replication," *Journal of Virology*, 5845-5851 (1996)

- * Burger et al., "Experimental Corneal Neovascularization: Biomicroscopic, Angiographic, and Morphologic Correlation," *Cornea* 4:35-41 (1985/1986)
- * Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," <u>Biochemistry</u> 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
- * Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," *Bioorganic & Medicinal Chemistry* 5:1999-2010 (1997)
- * Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)
- * Chiu et al., "siRNA function in RNAi: A chemical modification analysis," RNA, 9:1034-1048 (2003)
- * Choi et al., "Effect of Poly(ethylene glycol) Grafting on Polyethylenimine as a Gene Transfer Vector *in vitro*," *Bull. Korean Chem. Soc.*, 22, 46-52 (2001)
- Chun et al., "Effect of infusion of vasoactive intestinal peptide (VIP)-antisense oligodeoxynucleotide into the third cerebral ventricle above the hypothalamic cuprachiasmatic nucleus on the hyperglycemia caused by intracranial injection of 2-deoxy-D-glucose in rats," *Neuroscience Letters* 257:135-138 (1998)
- * Clemens et al., "The Double-Stranded RNA-Dependent Protein Kinase PKR: Structure and Function," *Journal of Interferon and Cytokine Research*, 17:503-524 (1997)
- * Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," <u>J. Am. Chem. Soc.</u> 113:6324-6326 (1991)
- * Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," <u>The Journ. of Biol. Chem.</u> 257:939-945 (1982)
- * Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal versus Subcutaneous Administration," Clinical Cancer Research 5:2330-2337 (1999)
- * d'Aldin et al., "Antisense oligonucleotides to the GluR2 AMPA receptor subunit modify excitatory synaptic transmission in vivo," *Molecular Brain Research* 55:151-164 (1998)

- * Diebold et al., "Mannose Polyethylenimine Conjugates for Targeted DNA Delivery into Dendritic Cells*," *The Journal of Biological Chemistry*, 274, 19087-19094 (1999)
- * Dryden et al., "The lack of specificity of neuropeptide Y (NPY) antisense oligodeoxynucleotides administered intracerebroventricularly in inhibiting food intake and NPY gene expression in the rat hypothalamus," *Journal of Endocrinology* 157:169-175 (1998)
- * Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," <u>Nucleic Acids Research</u> 18:6353-6359 (1990) [sometimes referred to as Seela and Kaiser]
- * Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," *Biopolymers* 48:39-55 (1998)
- * Edbauer et al., Resenilin and nicastrin regulate each other and determine amyloid β -peptide production via complex formation," *PNAS*, 99, 8666-8671 (2002)
- * Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," *Nature* 411:494-498 (2001)
- * Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in Drosophila Melanogaster Embryo Lysate," <u>The EMBO Journal</u> 20:6877-6888 (2001)
- * Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," Genes and Development 15:188-200 (2001)
- * Elkins and Rossi, "Ch. 2 Cellular Delivery of Ribozymes," in <u>Delivery Strategies</u> for Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220 (1995)
- * Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," *Cell Transplantation* 8:47-58 (1999)
- * Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and *In Vivo*, Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," Antisense and Nucleic Acid Drug Dev. 10:469-478 (2000)

- * Erbacher et al., "Transfection and physical properties of various sacccharide, poly(ethylene glycol), and antibody-derivatized polyethylenimines (PEI), *The Journal of Gene Medicine*, 1, 210-222 (1999) [sometimes incorrectly cited as pages 1-18]
- * Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," <u>J. Am. Chem. Soc.</u> 113:4000-4002 (1991)
- * Filion and Phillips, "Toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells," *Biochimica et Biophysica Acta* 1329:345-356 (1997)
- * Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in Caenorhabditis Elegans," Nature 391:806-811(1998)
- * Fire, "RNA-triggered Gene Silencing," <u>TIG</u> 15:358-363(1999)
- * Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]
- * Furgeson et al., "Modified Linear Polyethylenimine—Cholesterol Conjugates for DNA Complexation," *Bioconjugate Chem.*, 14, 840-847 (2003)
- * Futami et al., "Induction of apoptosis in HeLa cells with siRNA expression vector targeted against bcl-2," Nucleic Acids Research Supplement, 251-252 (2002)
- * GenBank Accession No. AB020693
- * GenBank Accession No. AF037412
- * GenBank Accession No. AF063658
- * Genbank Accession No. AF100308.1
- * GenBank Accession No. AJ430458
- * GenBank Accession No. D00239
- * GenBank Accession No. D11168
- * GenBank Accession No. D50483.1
- * GenBank Accession No. K02121

- * GenBank Accession No. L24917
- GenBank Accession No. L38318
- * GenBank Accession No. M16248
- * GenBank Accession No. M31724
- GenBank Accession No. NC_001345
- * GenBank Accession No. NC_001347
- * GenBank Accession No. NC_001353
- * GenBank Accession No. NC_001563
- * GenBank Accession No. NC_001781
- * GenBank Accession No. NM_001285
- * GenBank Accession No. NM_001982
- * GenBank Accession No. NM_002592.1
- * GenBank Accession No. NM 002667
- * GenBank Accession No. NM_002737
- GenBank Accession No. NM_003219
- Genbank Accession No. NM 003376.1
- GenBank Accession No. NM_004283
- * GenBank Accession No. NM_004448
- * GenBank Accession No. NM_005228
- * GenBank Accession No. NM_005235
- * GenBank Accession No. S82227
- * GenBank Accession No. U51188
- * GenBank Accession No. U86046

- GenBank Accession No. X01087
- GenBank Accession No. X02316
- * GenBank Accession No. X07203
- * GenBank Accession No. X60667
- * GenBank Accession No. XM_015620
- * GenBank Accession No. XM 033884
- * GenBank Accession No. XM_067723
- * Ghirnikar et al., "Chemokine inhibition in rat stab would brain injury using antisense oligodeoxynucleotides," *Neuroscience Letters* 247:21-24 (1998)
- * Godbey et al., "Poly(ethylenimine) and its role in gene delivery," *Journal of Controlled Release*, 60, 149-160 (1999)
- * Godbey et al., "Tracking the intracellular path of poly(ethylenimine)/DNA complexes for gene delivery," *Proc. Natl. Acad. Sci. USA*, 96, 5177-5181 (1999)
- * Gold et al., "Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)
- * Gold, "Axonal Regeneration of Sensory Nerves is Delayed by Continuous Intrathecal Infusion of Nerve Growth Factor," *Neuroscience* 76:1153-1158 (1997)
- * Gonzalez et al., "New Class of Polymers for the Delivery of Macromolecular Therapeutics," *Bioconjugate Chem.*, 10, 1068-1074 (1999)
- * Grant et al., "Insulin-like growth factor I acts as an angiogenic agent in rabbit cornea and retina: comparative studies with basic fibroblast growth factor," *Diabetologia* 36:282-291 (1993)
- * Hall et al., "Establishment and Maintenance of a Heterochromatin Domain," Science 297:2232-2237 (2002)
- * Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," *Science*, 286, 950-952 (1999)
- * Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in *Drosophila* Cells," Nature 404:293-296 (2000)

- * Haniu et al., "Characterization of Alzheimer's β-Secretase Protein BACE," *The Journal of Biological Chemistry*, 275, 21099-21106 (2000)
- * Harborth et al., "Sequence, Chemical, and Structural Variation of Small Interfering RNAs and Short Hairpin RNAs and the Effect on Mammalian Gene Silencing," Antisense and Nucleic Acid Drug Development, 13:83-105 (2003)
- * Hartmann et al., "Spontaneous and Cationic Lipid-Mediated Uptake of Antisense Oligonucleotides in Human Monocytes and Lymphocytes," *The Journal of Pharmacology and Experimental Therapeutics* 285:920-928 (1998)
- * Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," *Science* 287:820-825 (2000)
- * Hofland and Huang, "Formulation and Delivery of Nucleic Acids," *Handbook of Exp. Pharmacol.* 137:165-192 (1999)
- * Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," VCH, 331-417
- * Hussain et al., "Identification of a Novel Aspartic Protease (Asp 2) as β-Secretase," *Molecular and Cellular Neuroscience*, 14, 419-427 (1999)
- * Hutvagner and Zamore, "A MicroRNA in a Multiple-Turnover RNAi Enzyme Complex," Science 297:2056-2060 (2002)
- * Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the *let-7* Small Temporal RNA," <u>Science</u> 293:834-838 (2001)
- * International Search Report for PCT/US03/04710 mailed November 18, 2003
- * International Search Report for PCT/US03/05028 mailed October 17, 2003
- * International Search Report for PCT/US03/05346 mailed October 17, 2003
- * International Search Report mailed November 19, 2003 for PCT/US03/18911
- * Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm. Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
- * Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random Sequences Using an Anchored Substrate RNA," <u>Biochemical and Biophysical Research Communication</u> 214(2):403-409 (1995)

- Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic Oligonucleotides," <u>Tetrahedron Letters</u> 34:301-304 (1993) (sometimes mistakenly referred to as Jschke)
- * Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," Clinical Chemistry 45:1628-1650 (1999)
- * Jenuwein, "An RNA-Guided Pathway for the Epigenome," <u>Science</u> 297:2215-2218 (2002)
- * Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," *Fundam. Clin. Pharmacol.* 13:16-26 (1999)
- Joyce et al., "Amplification, mutation and selection of catalytic RNA," <u>Gene</u> 82:83-87 (1989)
- * Joyce, "Directed Molecular Evolution," <u>Scientific American</u> 267:90-97 (1992)
- * Karle et al., "Differential Changes in Induced Seizures After Hippocampal Treatment of Rats with an Antisense Oligodeoxynucleotide to the GABA_A Receptor γ2 Subunit," <u>Euro. Jour. of Pharmacology</u> 340:153-160 (1997)
- * Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," <u>Tetrahedron Letters</u> 39:1131-1134 (1998)
- * Kim et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth *in vivo*," <u>Nature</u> 362:841-844 (1993)
- * Koch et al., "Vascular Endothelial Growth Factor," *Journal of Immunology*, 152:4149-4156 (1994)
- * Koike et al., "Thimet Oligopeptidase Cleaves the Full-Length Alzheimer Amyloid Precursor Protein at a β-Secretase Cleavage Site in COS Cells," *J. Biochem.*, 126, 235-242 (1999)
- * Kronenwett et al., "Oligodeoxyribonucleotide Uptake in Primary Human Hematopoietic Cells is Enhanced by Cationic Lipids and Depends on the Hematopoietic Cell Subset," *Blood* 91:852-862 (1998)
- * Kumar and Ellington, "Artificial evolution and natural ribozymes," <u>FASEB J.</u> 9:1183-1195 (1995)

- * Kunath et al., "The structure of PEG-modified poly(ethylene imines) influences biodistribution and pharmacokinetics of their complexes with NF-kappaB decoy in mice.," Medline (Pharm Res.) 19(6): 810-817 (6/1/2002)
- * Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," Reviews in Molecular Biotechnology 74:27-38 (2000)
- * Kuwabara et al., "Allosterically Controllable Ribozymes with Biosensor Functions," Current Opinion in Chem. Biol. 4:669-677 (2000)
- Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial,"
 <u>Chemical Reviews</u> 95:2601-2627 (1995)
- * Lasic and Papahadjopoulos, "Liposomes Revisited," <u>Science</u> 267:1275-1276 (1995)
- * Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," ACS Symposium Series 752:184-192 (2000)
- * Lee and Lee, "Preparation of Cluster Glycosides of *N*-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," <u>Glyconjugates J.</u> 4:317-328 (1987)
- Lee et al., "Enhancing the Catalytic Repertoire of Nucleic Acids: A Systematic Study of Linker Length and Rigidity," <u>Nucleic Acids Research</u> 29:1565-1573 (2001)
- * Leirdal et al., "Gene silencing in mammalian cells by preformed small RNA duplexes," Biochemical and Biophysical Research Communications, 295, 744-748 (2002)
- * Lendlein et al., "Biodegradable, Elastic Shape-Memory Polymers for Potential Biomedical Applications," *Science*, 296, 1673-1676 (2002)
- * Lepri et al., "Effect of Low Molecular Weight Heparan Sulphate on Angiogenesis in the Rat Cornea after Chemical Cauterization," *Journal of Ocular Pharmacology* 10:273-281 (1994)
- * Lichner et al., "Double-stranded RNA-binding proteins could suppress RNA interference-mediated antiviral defences," *Journal of General Virology*, 84, 975-980 (2003)
- * Limbach et al., "Summary: the modified nucleosides of RNA," <u>Nucleic Acids</u> Research 22(12):2183-2196 (1994)

- * Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," *J. Am. Chem. Soc.* 120:8531-8532 (1998)
- * Lin et al., "A Novel mRNA-cRNA Interference Phenomenon for Silencing bcl-2 Expression in Human LNCaP Cells," Biochemical and Biophysical Research Communications, 281, 639-644 (2001)
- * Lin et al., "Human aspartic protease memapsin 2 cleaves the β-secretase siet of β-amyloid precursor protein," *PNAS*, 97, 1456-1460 (2000)
- * Lin et al., "Policing rogue genes," Nature, 402, 128-129 (1999)
- * Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," <u>J. Biol.</u> Chem. 270(42):24864-24870 (1995)
- * Liu et al., "Hydrodynamics-based transfection in animals by systemic administration of plasmid DNA," *Gene Therapy*, 6, 1258-1266 (1999)
- * Loakes, "The Applications of Universal DNA Base Analogues," <u>Nucleic Acids</u> <u>Research</u> 29:2437-2447 (2001)
- * Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," <u>Proc. Natl. Acad. Sci. USA</u> 91:6977-6981 (1994)
- * Ma and Wei, "Enhanced Delivery of Synthetic Oligonucleotides to Human Leukaemic Cells by Liposomes and Immunoliposomes," *Leukemia Research* 20:925-930 (1996)
- * Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," Biochemistry 32:1751-1758 (1993)
- * Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," <u>Nucleic Acids Research</u> 21:2585-2589 (1993)
- * Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," <u>Cell</u> 110:563-574 (2002)
- * Matulic-Adamic et al., "Functionalized Nucleoside 5'-triphosphates for In Vitro Selection of New Catalytic Ribonucleic Acids," <u>Bioorganic & Medicinal Chemistry</u> <u>Letters</u> 10:1299-1302 (2000)

- * Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," Molecular Membrane Biology 16:129-140 (1999)
- * McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" <u>Nucleosides & Nucleotides</u> 10:287-290 (1991)
- * McManus et al., "Gene Silencing Using Micro-RNA Designed Hairpins," RNA 8:842-850 (2002)
- * Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," <u>American Chemical Society</u>, pp. 24-39 (1994)
- Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," <u>Science</u> 256:992-996 (1992)
- * Mori et al., "Pigment epithelium-derived factor inhibits retinal and choroidal neovacularization," Journal of Cellular Physiology, 118(2) 253-263 (2001)
- * Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted Selection for Improved Cleavage," <u>Biochemistry</u> 33:1271-1277 (1994)
- * Noviello et al., "Autosomal Recessive Hypercholesterolemia Protein Interacts with and Regulates the Cell Surface Level of Alzheimer's Amyloid β Precursor Protein*," The Journal of Biological Chemistry, 278, 31843-31847 (2003)
- * Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell 107:309-321 (2001)
- * Ohno-Matsui et al., "Inducible Expression of Vascular Endothelial Growth Factor in Adult Mice Causes Severe Proliferative Retinopathy and Retinal Detachment," Am. J. Pathology, 160, 711-719 (2002)
- Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," <u>Biochimica et Biophysica Acta</u> 1238:86-90 (1995)
- * Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," <u>Biochemistry</u> 30:9914-9921 (1991)
- * O'Reilly et al., "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," Cell 79:315-328 (1994)

- * Orgis et al., "DNA/polyethylenimine transfection particles: Influence of ligands, polymer size, and PEGylation on internalization and gene expression," AAPS PharmSci., 3 (3) article 21 (http://www.pharmsci.org) p. 1- 11 (2001)
- * Ormerod et al., "Effects of Altering the Eicosanoid Precursor Pool on Neovascularization and Inflammation in the Alkali-burned Rabbit Cornea," American Journal of Pathology 137:1243-1252 (1990)
- * Pal-Bhadra et al., "Heterochromatic Silencing and HP1 Localizatin in Drosophila Are Dependent on the RNAi Machinery," Science, 303, 669-672 (2004)
- Pandey et al., "Role ov B61, the Ligand for the Eck Receptor Tyrosine Kinase, in TNF- α -Induced Angiogenesis," Science 268:567-569 (1995)
- * Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier *in vivo*," *Proc. Natl. Acad. Sci. USA* 92:5592-5596 (1995)
- * Parrish, "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," Molecular Cell 6:1077-1087 (2000)
- * Passaniti et al., "A Simple, Quantitative Method for Assessing Angiogenesis and Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and Fibroblast Growth Factor," *Laboratory Investigation* 67:519-528 (1992)
- * Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
- * Petersen et al., "Polyethylenimine-*graft*-Poly(ethylene glycol) Copolymers: Influence of Copolymer Block Structure on DNA Complexation and Biological Activities as Gene Delivery System, *Bioconjugate Chem.*, 13, 845-854 (2002)
- * Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," <u>Science</u> 253:314-317 (1991)
- * Pierce et al., "Vascular endothelial growth factor/vascular permeability factor expression in a mouse model of retinal neovascularization," *Proc. Natl. Acad. Sci. USA* 92:905-909 (1995)
- * Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," J. Med. Chem. 24:1388-1395 (1981)
- * Rajakumar et al., "Effects of Intrastriatal Infusion of D₂ Receptor Antisense Oligonucleotide on Apomorphine-Induced Behaviors in the Rat," <u>Synapse</u> 26:199-208 (1997)

- * Randall et al., "Clearance of replicating hepatitis C virus replicon RNAs in cell culture by small interfering RNAs," *PNAS*, 100, 235-240 (2003)
- * Reinhart and Bartel, "Small RNAs Correspond to Centromer Heterochromatic Repeats," <u>Science</u> 297:1831 (2002)
- * Reinhart et al., "MicroRNAs in Plants," <u>Genes & Development</u> 16:1616-1626 (2002)
- * Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA," <u>J. Am. Chem. Soc.</u> 113:5109-5111 (1991)
- * Saenger (ed), "Modified Nucleosides and Nucleotides; Nucleoside Di- and Triphosphates; Coenzymes and Antibiotics, (ch.7)" Principles of Nucleic Acid Structure 158-200 (1984)
- * Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," <u>Proc. Natl. Acad. Sci. USA</u> 94:4262-4266 (1997)
- * Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β -cyanoethyl protected ribonucleoside phosphoramidites," <u>Nucl Acids Res.</u> 18:5433-5441 (1990)
- * Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 23:941-949 (1999) [sometimes cited by RPI as Prog Neuropsychopharmacol Biol Psychiatry 23:941-949, 1999]
- * Schwarz et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," <u>Molecular Cell</u> 10:537-548 (2002)
- * Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," Nucleic Acids Research 15:3113-3129 (1987)
- Segarra et al., "Molecular characterization of the Enterococcus faecalis cytolysin activator," *Infection and Immunity*, 59, 4, 1239-1246 (1991) Database CAPLUS on STN, AN:1992:230597
- * Senger et al., "Vascular permeability factor (VPF, VEGF) in tumor biology," Cancer and Matastasis Reviews 12:303-324 (1993)
- * Shabarova et al., "Chemical ligation of DNA: The first non-enyzmatic assembly of a biologically active gene," <u>Nucleic Acids Research</u> 19:4247-4251 (1991)

- * Sharp et al., "RNAi and double-strand RNA," *Genes & Development*, 13:139-141 (1999)
- * Sheehan et al., "Biochemical properties of phosphonoacetate and thiophosphonoacetate oligodeoxyribonucleotides," *Nucleic Acids Research*, 31 (14), 4109-4118 (2003)
- * Shweiki et al., "Patterns of Expression of Vascular Endothelial Growth Factor (VEGF) and VEGF Receptors in Mice Suggest a Role in Hormonally Regulated Angiogenesis," *J. Clin. Invest.* 91:2235-2243 (1993)
- * Simantov et al., "Dopamine-Induced Apoptosis in Human Neuronal Cells: Inhibition by Nucleic Acids Antisense to the Dopamine Transporter," Neuroscience 74(1):39-50 (1996)
- * Sommer et al., "The Spread and Uptake Pattern of Intracerebrally Administered Oligonucleotides in Nerve and Glial Cell Populations of the Rat Brain," <u>Antisense & Nucleic Acid Drug Development</u> 8:75-85 (1998)
- * Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," Molecular Biology, Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being published in *Science*]
- * Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," <u>Current Opinion in Molecular Therapeutics</u> 2:100-105 (2000)
- * Szostak, "In Vitro Genes," <u>TIBS</u> 17:89-93 (1993)
- * Takahashi et al., "Markedly Increased Amounts of Messenger RNAs for Vascular Endothelial Growth Factor and Placenta Growth Factor in Renal Cell Carcinoma Associated with Angiogenesis," Cancer Research 54:4233-4237 (1994)
- * Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by in vitro selection," <u>RNA</u> 3:914-925 (1997)
- * Thomas et al., "Enhancing polyethylenimine's delivery of plasmid DNA into mammalian cells," *PNAS*, 99, 14640-14645 (2002)
- Turner et al., "Improved Parameters for Prediction of RNA Structure," <u>Cold Spring</u>
 <u>Harbor Symposia on Quantitative Biology</u> Volume LII, pp. 123-133 (1987)
- * Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," J. Am. Chem. Soc. 109:3783-3785 (1987)

- * Tuschl et al., "Small Interfering RNAs: A Revolutionary Tool for Analysis of Gene Function and Gene Therapy," Molecular Interventions, 295, 3, 158-167 (2002)
- * Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes & Development 3191-3197 (1999)
- * Tuschl, "RNA Interference and Small Interfering RNAs," <u>Chembiochem</u> 2:239-245 (2001)
- * Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," *Proc. Natl. Acad. Sci. USA* 96:7053-7058 (1999)
- * Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells in vivo," FEBS Letters 421:280-284 (1998)
- * Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle," Chemical Reviews 90:544-584 (1990)
- * Usman and Cedergren, "Exploiting the chemical synthesis of RNA," <u>TIBS</u> 17:334-339 (1992)
- * Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an *Escherichia coli* Formylmethoionine tRNA," <u>J. Am. Chem. Soc.</u> 109:7845-7854 (1987)
- * Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," <u>Nucleic Acids Syposium Series</u> 31:163-164 (1994)
- * Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by in Vitro Selection," <u>Biochemistry</u> 36:6495-6501 (1997)
- * Vassar et al., "β-Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," *Science* 286:735-741 (1999)
- * Verdel et al., "RNAi-Mediated Targeting ofHeterochromatin by the RITS Complex, Science, 303, 672-676 (2004)
- * Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," Annu. Rev. Biochem. 67:99-134 (1998)
- Volpe et al., "Regulation of Heterochromatic Silencing and Histone H3 Lysine-9 Methylation by RNAi," <u>Science</u> 297:1833-1837 (2002)

- * Waterhouse et al., "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," Proc. Natl. Acad. Sci. USA, 95, 13959-13964 (1998)
- * Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," <u>Nature Cell Biology</u> 2:70-75 (2000)
- * Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," <u>Nucleic Acids Research</u> 23(14):2677-2684 (1995)
- * Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," Methods in Molecular Biology 74:59-69 (1997)
- * Wu and Wu, "Receptor-mediated *in Vitro* Gene Transformation by a Soluble DNA Carrier System," <u>The Journ. of Biol. Chem.</u> 262:4429-4432 (1987)
- * Wu-Pong et al., "Nucleic Acid Drug Delivery, Part 2; Delivery to the Brain," BioPharm 32-38 (1999)
- * Yamada et al., "Nanoparticles for the delivery of genes and drugs to human hepatocytes," *Nature Biology, Published online: 29 June 2003, doi:10.1038/nbt843* (August 2003 Volume 21 Number 8 pp 885-890) (2003)
- * Yan et al., "Membrane-anchored Aspartyl Protease with Alzheimer's Disease β-Secretase Activity," Nature 402:533-537 (1999)
- * Yang et al., "Hydrodynamic injection of viral DNA: A mouse model of acute hepatitis B virus infection," PNAS, 99, 21, 13825-13830 (2002)
- * Zamore et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell 101:25-33 (2000)
- Ziche et al., "Angiogenesis Can Be Stimulated or Repressed In Vivo by a Change in GM3:GD3 Ganglioside Ratio," Laboratory Investigation 67:711-715 (1992)

* Zinnen et al., "Chemically Modified siRNAa: Potential Anti-viral Hepatitis Therapeutics" (Abstract) March 2004

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

Date: 8-10-04

Michael S. Greenfield

McDonnell Boehnen Hulbert & Berghoff LLP 300 South Wacker Drive, 32nd Floor Chicago, IL 60606

Telephone: 312-913-0001 Facsimile: 312-913-0002

26

	(0), 5 (2)			Sheet 1 of 27
FORM PTO-1449 (Rev. 2-32)	INFORMATION DIS STATEMENT BY A	SCLOSURE PPLICANT	Atty. Docket No. 03-465-D (400/151)	Serial No. 10/826,966
			Applicant: McSwiggen et al.	
			Filing Date: April 16, 2004	Group:

U.S. PATENT APPLICATION DOCUMENTS

Examiner Initial		Document Number	Filing Date	Name	Class	Subclass	Publication Date if Appropriate
	*	09/740,332	12/18/00	Blatt et al.			
	*	10/151,116	05/17/02	Matulic-Adamic et al.			
	*	10/201,394	08/13/01	Vargeese et al.			
	*	10/417,012	04/16/03	McSwiggen et al.			
	*	10/422,704	04/24/03	McSwiggen et al.			
	*	10/427,160	04/30/03	Vargeese et al.			
	*	10/444,853	05/23/03	McSwiggen et al.			
	*	10/652,791	08/29/03	McSwiggen et al.			
	*	10/693,059	10/23/03	McSwiggen et al.			
	*	10/720,448	11/24/03	McSwiggen et al.		-	
	*	10/727,780	12/03/03	Vaish et al.			
	*	60/082,404	04/20/98	Thompson et al.	-		
	*	60/358,580	02/20/02	Beigelman et al.			
	*	60/362,016	03/06/02	Matulic-Adamic et al.			
	*	60/363,124	03/11/02	Beigelman et al.			

EXAMINER	DATE CONSIDERED
	DATE CONCIDENCE

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	60/386,782	06/06/02	Beigelman et al.	
*	60/402,996	08/13/02	Usman et al.	
*	60/406,784	08/29/02	Beigelman et al.	
*	60/408,378	09/05/02	Beigelman et al.	
*	60/409,293	09/09/02	Beigelman et al.	
*	60/440,129	01/15/03	Beigelman et al.	
*	60/543,480	02/10/04	Jadhati et al.	
*	US 2001/0007666	01/05/99	Hoffman et al.	07/12/01
*	US 2002/0130430	12/29/00	Caster	09/19/02

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	*	5,138,045	08/11/92	Cook et al.			
	*	5,214,136	05/25/93	Lin et al.	•		
	*	5,334,711	08/02/94	Sproat			
	*	5,627,053	05/06/97	Usman et al.			
	*	5,631,360	05/20/97	Usman et al.			
	*	5,670,633	09/23/97	Cook et al.			

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
INFORMATION DISC STATEMENT BY API		(400/151)	
(Use several sheets if r	necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	5,672,695	09/30/97	Eckstein et al.	 	
*	5,716,824	02/10/98	Beigelman et al.	·	
*	5,792,847	08/11/98	Buhr et al.		
*	5,804,683	09/08/98	Usman et al.	 <u> </u>	
*	5,814,620	09/29/98	Robinson et al.	 	
*	5,831,071	11/03/98	Usman et al.		
*	5,854,038	12/29/98	Sullenger et al.		
*	5,889,136	03/30/99	Scaringe et al.	···	,
*	5,898,031	04/27/99	Crooke	· · · · · · · · · · · · · · · · · · ·	
*	5,998,203	12/07/99	Adamic et al.		
*	6,001,311	12/14/99	Brennan	-	
*	6,005,087	12/21/99	Cook et al.		
*	6,008,400	12/28/99	Scaringe et al.	 ··· · · · · · · · · · · · · · · · · ·	
*	6,054,576	04/25/00	Bellon et al.	 	
*	6,107,094	08/22/00	Crooke		
*	6,111,086	08/29/00	Scaringe et al.		
*	6,117,657	09/12/00	Usman et al.	····	
*	6,153,737	11/28/00	Manoharan et al.	 	
*	6,162,909	12/19/00	Bellon et al.	 	

EXAMINER	DATE CONSIDERED

					Sheet 4 of 27		
FORM PTO-1449 (Rev. 2-32)			epartment of Commerce nt and Trademark Office	Atty. Docket No.	Serial No.		
				03-465-D	10/826,966		
	INFORMAT STATEMEN	(400/151)					
	(Use several sheets if necessary)						
					Applicant:		
				Filing Date:	Group:		
				April 16, 2004			
T	T						
*	6,180,613	01/30/01	Kaplitt et al.				
al i		1					

1 -		T'			
6,180,613	01/30/01	Kaplitt et al.			
6,235,310	05/22/01	Wang et al.			
6,235,886	05/22/01	Manoharan et al.			
6,248,878	06/19/01	Adamic et al.			
6,300,074	10/09/01	Gold		· · · · · · · · · · · · · · · · · · ·	
6,303,773	10/16/01	Bellon et al.			
6,335,434	01/01/02	Guzaev et al.	· .		
6,353,098	03/05/02	Usman et al.	· ·		
6,362,323	03/26/02	Usman et al.			
6,395,713	05/28/02	Beigelman et al.		*	
6,437,117	08/20/02	Usman et al.		· ,···	
6,447,796	09/10/02	Vook et al.			
6,469,158	10/22/02	Usman et al.			
6,476,205	11/05/02	Buhr et al.		· · · ·	
6,506,559	06/14/03	Fire et al.			
6,528,631	03/04/03	Cook et al.			
6,586,524	07/01/03	Sagara			
6,617,156	09/09/03	Doucette-Stamm et al.			
	6,235,886 6,248,878 6,300,074 6,303,773 6,335,434 6,353,098 6,362,323 6,395,713 6,437,117 6,447,796 6,469,158 6,476,205 6,506,559 6,528,631 6,586,524	6,235,310 05/22/01 6,235,886 05/22/01 6,248,878 06/19/01 6,300,074 10/09/01 6,303,773 10/16/01 6,353,098 03/05/02 6,362,323 03/26/02 6,395,713 05/28/02 6,437,117 08/20/02 6,447,796 09/10/02 6,469,158 10/22/02 6,476,205 11/05/02 6,506,559 06/14/03 6,528,631 03/04/03 6,586,524 07/01/03	6,235,310 05/22/01 Wang et al. 6,235,886 05/22/01 Manoharan et al. 6,248,878 06/19/01 Adamic et al. 6,300,074 10/09/01 Gold 6,303,773 10/16/01 Bellon et al. 6,335,434 01/01/02 Guzaev et al. 6,353,098 03/05/02 Usman et al. 6,362,323 03/26/02 Usman et al. 6,437,117 08/20/02 Beigelman et al. 6,447,796 09/10/02 Vook et al. 6,469,158 10/22/02 Usman et al. 6,469,158 10/22/02 Usman et al. 6,506,559 06/14/03 Fire et al. 6,506,559 06/14/03 Fire et al. 6,586,524 07/01/03 Sagara	6,235,310 05/22/01 Wang et al. 6,235,886 05/22/01 Manoharan et al. 6,248,878 06/19/01 Adamic et al. 6,300,074 10/09/01 Gold 6,303,773 10/16/01 Bellon et al. 6,335,434 01/01/02 Guzaev et al. 6,353,098 03/05/02 Usman et al. 6,362,323 03/26/02 Usman et al. 6,395,713 05/28/02 Beigelman et al. 6,437,117 08/20/02 Usman et al. 6,447,796 09/10/02 Vook et al. 6,469,158 10/22/02 Usman et al. 6,476,205 11/05/02 Buhr et al. 6,506,559 06/14/03 Fire et al. 6,528,631 03/04/03 Cook et al. 6,586,524 07/01/03 Sagara	6,235,310 05/22/01 Wang et al. 6,235,886 05/22/01 Manoharan et al. 6,248,878 06/19/01 Adamic et al. 6,300,074 10/09/01 Gold 6,303,773 10/16/01 Bellon et al. 6,335,434 01/01/02 Guzaev et al. 6,353,098 03/05/02 Usman et al. 6,362,323 03/26/02 Usman et al. 6,395,713 05/28/02 Beigelman et al. 6,437,117 08/20/02 Usman et al. 6,447,796 09/10/02 Vook et al. 6,469,158 10/22/02 Usman et al. 6,476,205 11/05/02 Buhr et al. 6,506,559 06/14/03 Fire et al. 6,528,631 03/04/03 Cook et al. 6,586,524 07/01/03 Sagara

FOREIGN PATENT DOCUMENTS

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

					Translation		
	Document Number	Date	Country	Class	Subclass	Yes	No
 *	2001240375	03/16/01	AU (Graham et al.)				
	(Old Application No. 40375/01)						
*	2,359,180	08/03/00	CA (Kreutzer et al.)				· · · · · · · · · · · · · · · · · · ·
*	1144623 B1	01/29/02	EP (Kreutzer et al.)			-	
*	89/02439	03/23/89	WO (Arnold et al.)				
*	90/14090	11/29/90	WO (Gillespie et al.)				
*	91/03162	03/21/91	WO (Rossi et al.)	<u> </u>			
*	92/07065	04/30/92	WO (Eckstein et al.)				
*	93/15187	08/05/93	WO (Usman et al.)				
*	93/23569	11/25/93	WO (Draper et al.)				
*	94/01550	01/20/94	WO (Agrawal et al.)				
*	94/02595	02/03/94	WO (Sullivan et al.)				
*	95/06731	03/09/95	WO (Usman et al.)				
*	95/11910	05/04/95	WO (Dudycz et al.)				
*	96/10390	04/11/96	WO (Ansell et al.)				
*	96/10391	04/11/96	WO (Choi et al.)				

EXAMINER	DATE CONSIDERED

FORM PTO-144	9	U:	S. Department of Commerce	Atty. Docket No.	Serial No.
(Rev. 2-32)	•		Patent and Trademark Office	Atty. Docket 140.	Serial 140.
				03-465-D	10/826,966
	INFORMATI STATEMEN	(400/151)			
	(Use several	sheets if neces	sary)		
				Applicant:	
				McSwiggen et al.	
				Filing Date:	Group:
				April 16, 2004	
*	96/10392	04/11/96	WO (Holland et al.)		
*	97/26270	07/24/97	WO (Beigelman et al.)		
*	98/13526	04/02/98	WO (Woolf et al.)		
*	99/04819	02/04/99	WO (Klimuk)		
*	99/05094	02/04/99	WO (Beigelman et al.)		
*	99/07409	02/18/99	WO (Deschamps de Paillette et al.)		
*	99/14226	03/25/99	WO (Wengel et al.)		
*	99/31262	06/24/99	WO (Barry et al.)		
*	99/32619	07/01/99	WO (Fire et al.)		
*	99/49029	09/30/99	WO (Graham et al.)		
*	99/53050	10/21/99	WO (Waterhouse et al.)		
*	99/54459	10/28/99	WO (Thompson et al.)		
*	99/61631	12/02/99	WO (Heifetz et al.)		
*	00/01846	01/13/00	WO (Plaetinck et al.)		
*	00/17369	03/30/00	WO (Gurney et al.)		
*	00/44895	08/03/00	WO (Kreutzer et al.)		
*	00/44914	08/03/00	WO (Li et al.)		
*	00/49035	08/24/00	WO (Sheen)		
*	00/53722	09/14/00	WO (O'Hare and Normand)		

EXAMINER	DATE CONSIDERED

					Sheet 7 of 2
FORM PTO-144 (Rev. 2-32)	9		S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
	INFORMATIO STATEMENT	03-465-D (400/151)	10/826,966		
	(Use several sl	neets if neces	sary)		
				Applicant:	
				McSwiggen et al.	
				Filing Date:	Group:
				April 16, 2004	
*	00/63364	10/26/00	WO (Pachuk et al.)		
*	00/66604	11/09/00	WO (Wengel et al.)		
*	01/04313	01/18/01	WO (Satishchandran et al.)		
*	01/29058	04/26/01	WO (Mello et al.)		
*	01/36646	05/25/01	WO (Zernicka-Goetz et al.)		
*	01/38551	05/31/01	WO (Grossniklaus)		
*	01/42443	06/14/01	WO (Churikov et al.)		
*	01/49844	07/12/01	WO (Driscoll et al.)		
*	01/53475	07/26/01	WO (Cogoni et al.)		
*	01/68836	09/20/01	WO (Beach et al.)		
*	01/70944	09/27/01	WO (Honer et al.)		
*	01/70949	09/27/01	WO (Graham et al.)		
*	01/72774	10/04/01	WO (Deak et al.)		
*	01/75164	10/11/01	WO (Tuschl et al.)		
*	01/92513	12/06/01	WO (Arndt et al.)		
*	01/96584	12/20/01	WO (Mushegian et al.)		
*	02/15876	02/28/02	WO (Beigelman et al.)		
*	02/22636	03/21/02	WO (Bennett et al.)		
	02/38805	05/16/02	WO (Echeverri et al.)		

EXAMINER	DATE CONSIDERED

FORM PTO-144 (Rev. 2-32)	FORM PTO-1449 Rev. 2-32) U.S. Department of Commerce Patent and Trademark Office			Atty. Docket No. 03-465-D	Serial No. 10/826,966	
	INFORMATION STATEMENT (Use several si	(400/151)				
	(000 0010101 01	icolo ii ricoco	Sury)	Applicant:	1	
				McSwiggen et al.		
				Filing Date:	Group:	
				April 16, 2004		
*	02/44321	06/06/02	WO (Tuschl et al.)			
*	02/55692	07/18/02	WO (Kreutzer et al.)			
*	02/55693	07/18/02	WO (Kreutzer et al.)			
*	02/094185 (PCT/US02/15876)	11/28/02	WO (Beigelman et al.)			
*	03/024420	03/27/03	WO (Ahlheim et al.)			
*	03/046185	06/05/03	WO (Wang et al.)			
*	03/047518	06/12/03	WO (Wang et al.)			
*	03/064625	08/07/03	WO (Woolf et al.)			
*	03/064626	08/07/03	WO (Woolf et al.)			
*	03/070918 (PCT/US03/05346)	08/28/03	WO (McSwiggen et al.)			
*	03/074654 (PCT/US03/05028)	09/12/03	WO (McSwiggen et al.)			
*	04/013280	02/12/04	WO (Davidson et al.)			
	OTHER DOCU	MENTS (Incl	uding Author, Title, Date, Per	tinent Pages, Etc).		
*	* Adah et al., "Chemistry and Biochemistry of 2',5'-Oligoadenylate-Based Antisense Strategy," Current Medicinal Chemistry, 8, 1189-1212 (2001)					
	* Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," <u>Trends Cell Biol.</u> 2:139-144 (1992)					

EXAMINER	DATE CONSIDERED

Sheet 9 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office		Serial No.
•		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
·		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in		
	cultured neurons when coupled to a retro-inverso delivery peptide. The antisense activity		
	depresses the target mRNA and protein in magnocellular oxytocin neurons," <u>Nucleic Acids</u>		
	Research 26:4910-4916 (1998)		
*	Allshire, "RNAi and Heterochromatin - A Hushed-up Affair," <u>Science</u> 297:1818-1819 (2002)		
*	Andrews and Faller, "A rapid micropreparation technique for extraction of DNA-binding proteins from limiting numbers of mammalian cells," <i>Nucleic Acids Research</i> 19:2499 (1991)		
*	Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," Cell 22:611-620 (1980)		
*	Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent α1(I) Collagen by a Homologous Transcriptionally Self-Silenced Transgene," <i>Molecular and Cellular Biology</i> , 274-283 (1999)		
*	Bannai et al., "Effect of Injection of Antisense of Oligodeoxynucleotides of GAD Isozymes into Rat Ventromedial Hypothalamus on Food Intake and Locomotor Activity," <u>Brain</u> Research 784:305-315 (1998)		
*	Bannai et al., "Water-absorbent Polymer as a Carrier for a Discrete Deposit of Antisense Oligodeoxynucleotides in the Central Nervous System," <u>Brain Research Protocols</u> 3:83-87 (1998)		
*	Bartel and Szostak, "Isolation of New Ribozymes from a Large Pool of Random Sequences," Science 261:1411-1418 (1993)		
*	Basi et al., "Antagonistic Effects of β -Site Amyloid Precursor Prtein-cleaving Enzymes 1 and 2 on β -Amyloid Peptide Production in Cells*," <i>The Journal of Biological Chemistry</i> , 278, 31512-31520 (2003)		
*	Bass, "Double-Stranded RNA as a Template for Gene Silencing," <i>Cell</i> , 101, 235-238 (2000)		

EXAMINER	DATE CONSIDERED

Sheet 10 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office		Serial No.
,		03-465-D	10/826,966
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		(400/151)	
(U	se several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

	*	Bass, "The short answer," Nature 411:428-429 (2001)
	*	Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," Tetrahedron 49:1925-1963 (1993)
	*	Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," <u>Science</u> 257:635-641 (1992)
	*	Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," <u>The Journal of Biological Chemistry</u> 270:25702-25708 (1995)
	*	Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," Nucleosides & Nucleotides 16:951-954 (1997)
	*	Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," <u>Bioconjugate Chem.</u> 8:204-212 (1997)
	*	Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," Nature 409:363-366 (2001)
	*	Bettinger et al., "Size Reduction of Galactosylated PEI/DNA Complexes Improves Lectin-Mediated Gene Transfer into Hepatocytes," <i>Bioconjugate Chem.</i> , 10, 558-561 (1999)
_	*	Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>Journal of Pharmaceutical Sciences</i> 87:1308-1315 (1998)
	*	Boado, "Antisense drug delivery through the blood-brain barrier," <i>Advanced Drug Delivery Reviews</i> 15:73-107 (1995)
	*	Bongartz et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," <i>Nucleic Acids Research</i> 22:4681-4688 (1994)
	*	Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus iterative selection methods," <u>TIBTECH</u> 12:268-275 (1994)
	*	Breaker, "Are engineered proteins getting competition from RNA?" Current Opinion in Biotechnology 7:442-448 (1996)

EXAMINER	DATE CONSIDERED

Sheet 11 of 27

FORM PTO-1449 (Rev. 2-32)		U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
,			03-465-D	10/826,966
INFORMATION DISCLOSURE STATEMENT BY APPLICANT			(400/151)	
	(Use several sheets if ne	ecessary)		
			Applicant:	
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

*	Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," <i>Biotechnology and Bioengineering (Combinatorial Chemistry)</i> 61:33-45 (1998)
*	Broaddus et al., "Distribution and stability of antisense phosphorothioate oligonucleotides in rodent brain following direct intraparenchymal controlled-rate infusion," Neurosurg. Focus 3(5):Article 4 (1997)
*	Broaddus et al., "Distribution and stability of antisense phosphorothioate oligonucleotides in rodent brain following direct intraparenchymal controlled-rate infusion," <u>J Neurosurg</u> 88:734-742 (1998)
*	Brody and Gold, "Aptamers as therapeutic and diagnostic agents," <i>Reviews in Molecular Biotechnology</i> 74:5-13 (2000)
*	Buckwold et al., "Effects of a Naturally Occurring Mutation in the Hepatitis B Virus Basal Core Promoter on Precore Cene Expression and Viral Replication," <i>Journal of Virology</i> , 5845-5851 (1996)
*	Burger et al., "Experimental Corneal Neovascularization: Biomicroscopic, Angiographic, and Morphologic Correlation," <i>Cornea</i> 4:35-41 (1985/1986)
*	Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," <u>Biochemistry</u> 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
*	Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," <i>Bioorganic & Medicinal Chemistry</i> 5:1999-2010 (1997)
*	Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)
*	Chiu et al., "siRNA function in RNAi: A chemical modification analysis," RNA, 9:1034-1048 (2003)
*	Choi et al., "Effect of Poly(ethylene glycol) Grafting on Polyethylenimine as a Gene Transfer Vector in vitro," Bull. Korean Chem. Soc., 22, 46-52 (2001)

EXAMINER	DATE CONSIDERED

Sheet 12 of 27

FORM PTO-1449 (Rev. 2-32)	U	J.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
			03-465-D	10/826,966
	INFORMATION DISCLOS STATEMENT BY APPLIC		(400/151)	
	(Use several sheets if nece	essary)		
			Applicant:	
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

	*	Chun et al., "Effect of infusion of vasoactive intestinal peptide (VIP)-antisense oligodeoxynucleotide into the third cerebral ventricle above the hypothalamic
·		cuprachiasmatic nucleus on the hyperglycemia caused by intracranial injection of 2-deoxy-D-glucose in rats," <i>Neuroscience Letters</i> 257:135-138 (1998)
	*	Clemens et al., "The Double-Stranded RNA-Dependent Protein Kinase PKR: Structure and Function," <i>Journal of Interferon and Cytokine Research</i> , 17:503-524 (1997)
	*	Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," <u>J. Am. Chem. Soc.</u> 113:6324-6326 (1991)
	*	Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," The Journ. of Biol. Chem. 257:939-945 (1982)
	*	Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal <i>versus</i> Subcutaneous Administration," <i>Clinical Cancer Research</i> 5:2330-2337 (1999)
	*	d'Aldin et al., "Antisense oligonucleotides to the GluR2 AMPA receptor subunit modify excitatory synaptic transmission in vivo," <i>Molecular Brain Research</i> 55:151-164 (1998)
	*	Diebold et al., "Mannose Polyethylenimine Conjugates for Targeted DNA Delivery into Dendritic Cells*," <i>The Journal of Biological Chemistry</i> , 274, 19087-19094 (1999)
	*	Dryden et al., "The lack of specificity of neuropeptide Y (NPY) antisense oligodeoxynucleotides administered intracerebroventricularly in inhibiting food intake and NPY gene expression in the rat hypothalamus," <i>Journal of Endocrinology</i> 157:169-175 (1998)
	*	Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," <u>Nucleic Acids Research</u> 18:6353-6359 (1990) [sometimes referred to as Seela and Kaiser]
	*	Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," <i>Biopolymers</i> 48:39-55 (1998)

	- 4
EXAMINER	DATE CONSIDERED

Sheet 13 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(4.2.1. 2.2.)		03-465-D	10/826,966
**	RMATION DISCLOSURE EMENT BY APPLICANT	(400/151)	
(Use se	everal sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Emerich et al., "Biocompatability of Poly (DL-Lactide- <i>co</i> -Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," <u>Antisense and Nucleic Acid Drug Dev.</u> 10:469-478 (2000) Erbacher et al., "Transfection and physical properties of various sacccharide, poly(ethylene glycol), and antibody-derivatized polyethylenimines (PEI), <i>The Journal of Gene Medicine</i> , 1, 210-222 (1999) [sometimes incorrectly cited as pages 1-18] Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," <u>J. Am. Chem. Soc.</u> 113:4000-4002 (1991) Filion and Phillips, "Toxicity and immunomodulatory activity of liposomal vectors
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," Antisense and Nucleic Acid Drug Dev. 10:469-478 (2000) Erbacher et al., "Transfection and physical properties of various sacccharide, poly(ethylene glycol), and antibody-derivatized polyethylenimines (PEI), <i>The Journal of Gene Medicine</i> , 1, 210-222 (1999) [sometimes incorrectly cited as pages 1-18]
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," <u>Antisense and Nucleic Acid Drug Dev.</u> 10:469-478 (2000) Erbacher et al., "Transfection and physical properties of various sacccharide, poly(ethylene glycol), and antibody-derivatized polyethylenimines (PEI), <i>The Journal of</i>
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," Antisense and Nucleic Acid Drug Dev. 10:469-478 (2000) Erbacher et al., "Transfection and physical properties of various sacccharide,
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," Antisense and Nucleic Acid Drug Dev. 10:469-478 (2000)
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In Vivo</i> , Using β-Cyclodextrin-Adamantane-Oligonucleotide Conjugates," Antisense and
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes Implanted Into the Brain," <i>Cell Transplantation</i> 8:47-58 (1999) Epa et al., "Downregulation of the p75 Neurotrophin Receptor in Tissue Culture and <i>In</i>
*	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes
*	
	Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220 (1995)
*	Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in <u>Delivery Strategies for</u>
*	Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," Genes and Development 15:188-200 (2001)
	Melanogaster Embryo Lysate," The EMBO Journal 20:6877-6888 (2001)
*	Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in Drosophila
	mammalian cells," <i>Nature</i> 411:494-498 (2001)
	Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured
*	Edbauer et al., Resenilin and nicastrin regulate each other and determine amyloid β - peptide production via complex formation," <i>PNAS</i> , 99, 8666-8671 (2002)
	*

EXAMINER	DATE CONSIDERED
	BATTE GOTTOIDETED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
INFORMATION DISCL STATEMENT BY APP		(400/151)	
(Use several sheets if n	ecessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

II		
	*	Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]
	*	Furgeson et al., "Modified Linear Polyethylenimine—Cholesterol Conjugates for DNA
		Complexation," Bioconjugate Chem., 14, 840-847 (2003)
	*	Futami et al., "Induction of apoptosis in HeLa cells with siRNA expression vector targeted
		against bcl-2," Nucleic Acids Research Supplement, 251-252 (2002)
	*	GenBank Accession No. AB020693
 	*	GenBank Accession No. AF037412
	*	
	*	GenBank Accession No. AF063658
	*	Genbank Accession No. AF100308.1
		GenBank Accession No. AJ430458
	*	GenBank Accession No. D00239
	*	GenBank Accession No. D11168
	*	GenBank Accession No. D50483.1
	*	GenBank Accession No. K02121
	*	GenBank Accession No. L24917
	*	GenBank Accession No. L38318
	*	GenBank Accession No. M16248
	*	GenBank Accession No. M31724
	*	GenBank Accession No. NC 001345
	*	GenBank Accession No. NC 001347
	*	GenBank Accession No. NC 001353
	*	GenBank Accession No. NC 001563
	*	GenBank Accession No. NC 001781
	 	GenBank Accession No. NM 001285
	*	GenBank Accession No. NM 001982
		CONDUMN / 1000331011 140. 14141_00 1302

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office		Serial No.
,		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	GenBank Accession No. NM_002592.1
*	GenBank Accession No. NM_002667
*	GenBank Accession No. NM_002737
*	GenBank Accession No. NM_003219
*	Genbank Accession No. NM_003376.1
*	GenBank Accession No. NM_004283
*	GenBank Accession No. NM_004448
*	GenBank Accession No. NM_005228
*	GenBank Accession No. NM_005235
*	GenBank Accession No. S82227
*	GenBank Accession No. U51188
*	GenBank Accession No. U86046
*	GenBank Accession No. X01087
*	GenBank Accession No. X02316
*	GenBank Accession No. X07203
*	GenBank Accession No. X60667
*	GenBank Accession No. XM_015620
*	GenBank Accession No. XM_033884
*	GenBank Accession No. XM_067723
*	Ghirnikar et al., "Chemokine inhibition in rat stab would brain injury using antisense
	oligodeoxynucleotides," Neuroscience Letters 247:21-24 (1998)
*	Godbey et al., "Poly(ethylenimine) and its role in gene delivery," Journal of Controlled
	Release, 60, 149-160 (1999)
*	Godbey et al., "Tracking the intracellular path of poly(ethylenimine)/DNA complexes for
	gene delivery," <i>Proc. Natl. Acad. Sci. USA,</i> 96, 5177-5181 (1999)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)		U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
,			03-465-D	10/826,966
	INFORMATION DISCL STATEMENT BY APP		(400/151)	
	(Use several sheets if ne	ecessary)		
			Applicant:	
			McSwiggen et al.	_
			Filing Date:	Group:
			April 16, 2004	

*	Gold et al., "Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)
*	Gold, "Axonal Regeneration of Sensory Nerves is Delayed by Continuous Intrathecal Infusion of Nerve Growth Factor," <i>Neuroscience</i> 76:1153-1158 (1997)
*	Gonzalez et al., "New Class of Polymers for the Delivery of Macromolecular Therapeutics," <i>Bioconjugate Chem.,</i> 10, 1068-1074 (1999)
*	Grant et al., "Insulin-like growth factor I acts as an angiogenic agent in rabbit cornea and retina: comparative studies with basic fibroblast growth factor," <i>Diabetologia</i> 36:282-291 (1993)
*	Hall et al., "Establishment and Maintenance of a Heterochromatin Domain," <u>Science</u> 297:2232-2237 (2002)
*	Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," <i>Science</i> , 286, 950-952 (1999))
*	Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in <i>Drosophila</i> Cells," Nature 404:293-296 (2000)
*	Haniu et al., "Characterization of Alzheimer's β-Secretase Protein BACE," The Journal of Biological Chemistry, 275, 21099-21106 (2000)
*	Harborth et al., "Sequence, Chemical, and Structural Variation of Small Interfering RNAs and Short Hairpin RNAs and the Effect on Mammalian Gene Silencing," Antisense and Nucleic Acid Drug Development, 13:83-105 (2003)
*	Hartmann et al., "Spontaneous and Cationic Lipid-Mediated Uptake of Antisense Oligonucleotides in Human Monocytes and Lymphocytes," <i>The Journal of Pharmacology and Experimental Therapeutics</i> 285:920-928 (1998)
*	Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," Science 287:820-825 (2000)

EXAMINER	DATE CONSIDERED

Sheet 17 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
,		03-465-D	10/826,966
INFORMATION D STATEMENT BY		(400/151)	
(Use several sheet	s if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

	*	Hofland and Huang, "Formulation and Delivery of Nucleic Acids," <i>Handbook of Exp. Pharmacol.</i> 137:165-192 (1999)
 	+	
		Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic
		Methods," <u>VCH</u> , 331-417
	*	Hussain et al., "Identification of a Novel Aspartic Protease (Asp 2) as β-Secretase,"
		Molecular and Cellular Neuroscience, 14, 419-427 (1999)
	*	Hutvagner and Zamore, "A MicroRNA in a Multiple-Turnover RNAi Enzyme Complex,"
		<u>Science</u> 297:2056-2060 (2002)
	*	Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the
		Maturation of the let-7 Small Temporal RNA," Science 293:834-838 (2001)
	*	International Search Report for PCT/US03/04710 mailed November 18, 2003
	*	International Search Report for PCT/US03/05028 mailed October 17, 2003
	*	International Search Report for PCT/US03/05346 mailed October 17, 2003
	*	International Search Report mailed November 19, 2003 for PCT/US03/18911
	*	Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene
		glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm.
		Rull 43:1005 1011 (1005) (mistakonly referred to as labituatest)
	*	Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
		Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random Sequences
		Using an Anchored Substrate RNA," Biochemical and Biophysical Research
		Communication 214(2):403-409 (1995)
	*	Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic
		Oligonucleotides," <u>Tetrahedron Letters</u> 34:301-304 (1993) (sometimes mistakenly referred
		to as Jschke)
	*	
		Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in
ļ		Diagnostics," Clinical Chemistry 45:1628-1650 (1999)
	*	Jenuwein, "An RNA-Guided Pathway for the Epigenome," Science 297:2215-2218 (2002)

EXAMINER	DATE CONSIDERED

Sheet 18 of 27

FORM PTO-1449 (Rev. 2-32)		J.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
,			03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT		(400/151)	
(1	Use several sheets if nece	essary)		
			Applicant:	
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

*	Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," <i>Fundam. Clin. Pharmacol.</i> 13:16-26 (1999)
*	Joyce et al., "Amplification, mutation and selection of catalytic RNA," <u>Gene</u> 82:83-87 (1989)
*	Joyce, "Directed Molecular Evolution," Scientific American 267:90-97 (1992)
*	Karle et al., "Differential Changes in Induced Seizures After Hippocampal Treatment of Rats with an Antisense Oligodeoxynucleotide to the GABA _A Receptor y2 Subunit," <u>Euro.</u> <u>Jour. of Pharmacology</u> 340:153-160 (1997)
*	Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," <u>Tetrahedron Letters</u> 39:1131-1134 (1998)
*	Kim et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth <i>in vivo</i> ," <u>Nature</u> 362:841-844 (1993)
*	Koch et al., "Vascular Endothelial Growth Factor," <i>Journal of Immunology</i> , 152:4149-4156 (1994)
*	Koike et al., "Thimet Oligopeptidase Cleaves the Full-Length Alzheimer Amyloid Precursor Protein at a β -Secretase Cleavage Site in COS Cells," <i>J. Biochem.</i> , 126, 235-242 (1999)
*	Kronenwett et al., "Oligodeoxyribonucleotide Uptake in Primary Human Hematopoietic Cells is Enhanced by Cationic Lipids and Depends on the Hematopoietic Cell Subset," <i>Blood</i> 91:852-862 (1998)
*	Kumar and Ellington, "Artificial evolution and natural ribozymes," <u>FASEB J.</u> 9:1183-1195 (1995)
*	Kunath et al., "The structure of PEG-modified poly(ethylene imines) influences biodistribution and pharmacokinetics of their complexes with NF-kappaB decoy in mice.," <i>Medline (Pharm Res.)</i> 19(6): 810-817 (6/1/2002)
*	Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," <i>Reviews in Molecular Biotechnology</i> 74:27-38 (2000)

ſ		
	EXAMINER	DATE CONSIDERED
l		

Sheet 19 of 27

FORM PTO-1449 (Rev. 2-32)		epartment of Commerce nt and Trademark Office	Atty. Docket No.	Serial No.
,			03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT		(400/151)	
	(Use several sheets if necessary	')		
			Applicant:	
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

*	Kuwabara et al., "Allosterically Controllable Ribozymes with Biosensor Functions," Current
	Opinion in Chem. Biol. 4:669-677 (2000)
*	Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," Chemical
	Reviews 95:2601-2627 (1995)
*	Lasic and Papahadjopoulos, "Liposomes Revisited," Science 267:1275-1276 (1995)
*	Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of
 	Macromolecules," ACS Symposium Series 752:184-192 (2000)
*	Lee and Lee, "Preparation of Cluster Glycosides of N-Acetylgalactosamine That Have
	Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific
	Receptor," Glyconjugates J. 4:317-328 (1987)
*	Lee et al., "Enhancing the Catalytic Repertoire of Nucleic Acids: A Systematic Study of
	Linker Length and Rigidity," Nucleic Acids Research 29:1565-1573 (2001)
*	Leirdal et al., "Gene silencing in mammalian cells by preformed small RNA duplexes,"
 	Biochemical and Biophysical Research Communications, 295, 744-748 (2002)
*	Lendlein et al., "Biodegradable, Elastic Shape-Memory Polymers for Potential Biomedical Applications," <i>Science</i> , 296, 1673-1676 (2002)
*	Lepri et al., "Effect of Low Molecular Weight Heparan Sulphate on Angiogenesis in the
	Rat Cornea after Chemical Cauterization," Journal of Ocular Pharmacology 10:273-281
	(1994)
*	Lichner et al., "Double-stranded RNA-binding proteins could suppress RNA interference-
	mediated antiviral defences," Journal of General Virology, 84, 975-980 (2003)
*	Limbach et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Research
	22(12):2183-2196 (1994)
*	Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in
	Helical Nucleic Acid," J. Am. Chem. Soc. 120:8531-8532 (1998)

EXAMINER	DATE CONSIDERED
<u>'</u>	

Sheet 20 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
•		03-465-D	10/826,966
INFORMATION DISC STATEMENT BY API		(400/151)	
(Use several sheets if r	necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Lin et al., "A Novel mRNA-cRNA Interference Phenomenon for Silencing bcl-2 Expression in Human LNCaP Cells," Biochemical and Biophysical Research Communications, 281, 639-644 (2001)
*	Lin et al., "Human aspartic protease memapsin 2 cleaves the β -secretase siet of β -amyloid precursor protein," <i>PNAS</i> , 97, 1456-1460 (2000)
*	Lin et al., "Policing rogue genes," Nature, 402, 128-129 (1999)
*	Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," J. Biol. Chem. 270(42):24864-24870 (1995)
*	Liu et al., "Hydrodynamics-based transfection in animals by systemic administration of plasmid DNA," <i>Gene Therapy,</i> 6, 1258-1266 (1999)
*	Loakes, "The Applications of Universal DNA Base Analogues," <u>Nucleic Acids Research</u> 29:2437-2447 (2001)
*	Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," <u>Proc. Natl. Acad. Sci. USA</u> 91:6977-6981 (1994)
*	Ma and Wei, "Enhanced Delivery of Synthetic Oligonucleotides to Human Leukaemic Cells by Liposomes and Immunoliposomes," <i>Leukemia Research</i> 20:925-930 (1996)
*	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," Biochemistry 32:1751-1758 (1993)
*	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," Nucleic Acids Research 21:2585-2589 (1993)
*	Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," Cell 110:563-574 (2002)
*	Matulic-Adamic et al., "Functionalized Nucleoside 5'-triphosphates for In Vitro Selection of New Catalytic Ribonucleic Acids," <u>Bioorganic & Medicinal Chemistry Letters</u> 10:1299-1302 (2000)

EXAMINER	DATE CONSIDERED

Sheet 21 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
	NFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
(1	Jse several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," Molecular Membrane Biology 16:129-140 (1999)
*	McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" Nucleosides & Nucleotides 10:287-290 (1991)
*	McManus et al., "Gene Silencing Using Micro-RNA Designed Hairpins," RNA 8:842-850 (2002)
 *	Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," <u>American</u> <u>Chemical Society</u> , pp. 24-39 (1994)
*	Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," Science 256:992-996 (1992)
*	Mori et al., "Pigment epithelium-derived factor inhibits retinal and choroidal neovacularization," Journal of Cellular Physiology, 118(2) 253-263 (2001)
*	Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted Selection for Improved Cleavage," Biochemistry 33:1271-1277 (1994)
*	Noviello et al., "Autosomal Recessive Hypercholesterolemia Protein Interacts with and Regulates the Cell Surface Level of Alzheimer's Amyloid β Precursor Protein*," <i>The Journal of Biological Chemistry</i> , 278, 31843-31847 (2003)
*	Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell 107:309-321 (2001)
*	Ohno-Matsui et al., "Inducible Expression of Vascular Endothelial Growth Factor in Adult Mice Causes Severe Proliferative Retinopathy and Retinal Detachment," <i>Am. J. Pathology</i> , 160, 711-719 (2002)
 *	Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," <u>Biochimica et Biophysica Acta</u> 1238:86-90 (1995)
*	Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," <u>Biochemistry</u> 30:9914-9921 (1991)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office		Serial No.
,		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
(Use several sheets if necessary)		
		Applicant:	_
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

* O'Reilly et al., "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the
 Suppression of Metastases by a Lewis Lung Carcinoma," Cell 79:315-328 (1994)
* Orgis et al., "DNA/polyethylenimine transfection particles: Influence of ligands, polymer
size, and PEGylation on internalization and gene expression," AAPS PharmSci., 3 (3)
 article 21 (http://www.pharmsci.org) p. 1- 11 (2001)
* Ormerod et al., "Effects of Altering the Eicosanoid Precursor Pool on Neovascularization
and Inflammation in the Alkali-burned Rabbit Cornea," American Journal of Pathology
 137:1243-1252 (1990)
* Pal-Bhadra et al., "Heterochromatic Silencing and HP1 Localizatin in Drosophila Are
Dependent on the RNAi Machinery," Science, 303, 669-672 (2004)
* Pandey et al., "Role ov B61, the Ligand for the Eck Receptor Tyrosine Kinase, in TNF-α-
Induced Angiogenesis," Science 268:567-569 (1995)
* Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid
analogue through the blood-brain barrier in vivo," Proc. Natl. Acad. Sci. USA 92:5592-
5596 (1995)
* Parrish, "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two
Trigger Strands in RNA Interference," Molecular Cell 6:1077-1087 (2000)
* Passaniti et al., "A Simple, Quantitative Method for Assessing Angiogenesis and
Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and
Fibroblast Growth Factor," Laboratory Investigation 67:519-528 (1992)
* Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity,"
Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
* Petersen et al., "Polyethylenimine-graft-Poly(ethylene glycol) Copolymers: Influence of
Copolymer Block Structure on DNA Complexation and Biological Activities as Gene
Delivery System, Bioconjugate Chem., 13, 845-854 (2002)
* Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified
Hammerhead Ribozymes," Science 253:314-317 (1991)

EXAMINER	DATE CONSIDERED

Sheet 23 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department Patent and Tra	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Pierce et al., "Vascular endothelial growth factor/vascular permeability factor expression in a mouse model of retinal neovascularization," <i>Proc. Natl. Acad. Sci. USA</i> 92:905-909
	(1995)
*	Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and
 *	Organs," J. Med. Chem. 24:1388-1395 (1981)
•	Rajakumar et al., "Effects of Intrastriatal Infusion of D ₂ Receptor Antisense
 _	Oligonucleotide on Apomorphine-Induced Behaviors in the Rat," Synapse 26:199-208 (1997)
*	Randall et al., "Clearance of replicating hepatitis C virus replicon RNAs in cell culture by
	small interfering RNAs," PNAS, 100, 235-240 (2003)
*	Reinhart and Bartel, "Small RNAs Correspond to Centromer Heterochromatic Repeats,"
	Science 297:1831 (2002)
*	Reinhart et al., "MicroRNAs in Plants," Genes & Development 16:1616-1626 (2002)
*	Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the
	Recognition of Structured RNA," J. Am. Chem. Soc. 113:5109-5111 (1991)
*	Saenger (ed), "Modified Nucleosides and Nucleotides; Nucleoside Di- and Triphosphates;
	Coenzymes and Antibiotics, (ch.7)" Principles of Nucleic Acid Structure 158-200 (1984)
*	Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," Proc. Natl. Acad.
 	<u>Sci. USA</u> 94:4262-4266 (1997)
*	Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β-
	cyanoethyl protected ribonucleoside phosphoramidites," <u>Nucl Acids Res.</u> 18:5433-5441
	(1990)
*	Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro,"
	Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 23:941-949 (1999) [sometimes cited by
	RPI as Prog Neuropsychopharmacol Biol Psychiatry 23:941-949, 1999]
*	Schwarz et al., "Evidence that siRNAs Function as Guides, Not Primers, in the Drosophila
	and Human RNAi Pathways," Molecular Cell 10:537-548 (2002)

EXAMINER	DATE CONSIDERED

Sheet 24 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
,		03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	(400/151)	
	(Use several sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside
 	substitute," Nucleic Acids Research 15:3113-3129 (1987)
*	Segarra et al., "Molecular characterization of the Enterococcus faecalis cytolysin
	activator," Infection and Immunity, 59, 4, 1239-1246 (1991) Database CAPLUS on STN,
	AN:1992:230597
*	Senger et al., "Vascular permeability factor (VPF, VEGF) in tumor biology," Cancer and
	Matastasis Reviews 12:303-324 (1993)
*	Shabarova et al., "Chemical ligation of DNA: The first non-enyzmatic assembly of a
	biologically active gene," Nucleic Acids Research 19:4247-4251 (1991)
*	Sharp et al., "RNAi and double-strand RNA," Genes & Development, 13:139-141 (1999)
*	Sheehan et al., "Biochemical properties of phosphonoacetate and thiophosphonoacetate
	oligodeoxyribonucleotides," Nucleic Acids Research, 31 (14), 4109-4118 (2003)
*	Shweiki et al., "Patterns of Expression of Vascular Endothelial Growth Factor (VEGF) and
	VEGF Receptors in Mice Suggest a Role in Hormonally Regulated Angiogenesis," J. Clin.
	Invest. 91:2235-2243 (1993)
*	Simantov et al., "Dopamine-Induced Apoptosis in Human Neuronal Cells: Inhibition by
	Nucleic Acids Antisense to the Dopamine Transporter," Neuroscience 74(1):39-50 (1996)
*	Sommer et al., "The Spread and Uptake Pattern of Intracerebrally Administered
	Oligonucleotides in Nerve and Glial Cell Populations of the Rat Brain," Antisense &
:	Nucleic Acid Drug Development 8:75-85 (1998)
*	Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," Molecular
	Biology, Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being
	published in Science]
*	Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," Current Opinion in Molecular
	<u>Therapeutics</u> 2:100-105 (2000)
*	Szostak, "In Vitro Genes," TIBS 17:89-93 (1993)

EXAMINER	DATE CONSIDERED

Sheet 25 of 27

FORM PTO-1449 (Rev. 2-32)		partment of Commerce	Atty. Docket No.	Serial No.
			03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT		(400/151)	
	(Use several sheets if necessary)			
			Applicant:	
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

	_	Takahashi et al., "Markedly Increased Amounts of Messenger RNAs for Vascular
	ļ ļ	Endothelial Growth Factor and Placenta Growth Factor in Renal Cell Carcinoma
		Associated with Angiogenesis," Cancer Research 54:4233-4237 (1994)
	*	Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by in vitro
		selection," RNA 3:914-925 (1997)
	*	Thomas et al., "Enhancing polyethylenimine's delivery of plasmid DNA into mammalian
		cells," PNAS, 99, 14640-14645 (2002)
	*	Turner et al., "Improved Parameters for Prediction of RNA Structure," Cold Spring Harbor
		Symposia on Quantitative Biology Volume LII, pp. 123-133 (1987)
	*	Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs,"
		<u>J. Am. Chem. Soc.</u> 109:3783-3785 (1987)
	*	Tuschl et al., "Small Interfering RNAs: A Revolutionary Tool for Analysis of Gene Function
		and Gene Therapy," Molecular Interventions, 295, 3, 158-167 (2002)
	*	Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes &
L		<u>Development</u> 3191-3197 (1999)
	*	Tuschl, "RNA Interference and Small Interfering RNAs," Chembiochem 2:239-245 (2001)
	*	Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered
		i.p. cross the blood-brain barrier and specifically reduce gene expression," Proc. Natl.
		Acad. Sci. USA 96:7053-7058 (1999)
	*	Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter
		neuronal cells in vivo," FEBS Letters 421:280-284 (1998)
	*	Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle,"
		<u>Chemical Reviews</u> 90:544-584 (1990)
	*	Usman and Cedergren, "Exploiting the chemical synthesis of RNA," TIBS 17:334-339
		(1992)

EXAMINER	DATE CONSIDERED

Sheet 26 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Co Patent and Tradema		Atty. Docket No.	Serial No.
,			03-465-D	10/826,966
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT		(400/151)	
	(Use several sheets if necessary)			
		Applicant:		
			McSwiggen et al.	
			Filing Date:	Group:
			April 16, 2004	

*	Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an <i>Escherichia coli</i> Formylmethoionine tRNA," J. Am. Chem. Soc. 109:7845-7854 (1987)
*	Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," Nucleic Acids Syposium Series 31:163-164 (1994)
*	Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by in Vitro Selection," Biochemistry 36:6495-6501 (1997)
*	Vassar et al., "β-Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," <i>Science</i> 286:735-741 (1999)
*	Verdel et al., "RNAi-Mediated Targeting ofHeterochromatin by the RITS Complex, Science, 303, 672-676 (2004)
*	Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," Annu. Rev. Biochem. 67:99-134 (1998)
*	Volpe et al., "Regulation of Heterochromatic Silencing and Histone H3 Lysine-9 Methylation by RNAi," Science 297:1833-1837 (2002)
*	Waterhouse et al., "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," Proc. Natl. Acad. Sci. USA, 95, 13959-13964 (1998)
 *	Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," Nature Cell Biology 2:70-75 (2000)
*	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," Nucleic Acids Research 23(14):2677-2684 (1995)
*	Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," Methods in Molecular Biology 74:59-69 (1997)
*	Wu and Wu, "Receptor-mediated <i>in Vitro</i> Gene Transformation by a Soluble DNA Carrier System," The Journ. of Biol. Chem. 262:4429-4432 (1987)

EXAMINER	DATE CONSIDERED

Sheet 27 of 27

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
		03-465-D	10/826,966
	TION DISCLOSURE NT BY APPLICANT	(400/151)	
(Use severa	sheets if necessary)		
		Applicant:	
		McSwiggen et al.	
		Filing Date:	Group:
		April 16, 2004	

*	Wu-Pong et al., "Nucleic Acid Drug Delivery, Part 2; Delivery to the Brain," <u>BioPharm</u> 32-38 (1999)
*	Yamada et al., "Nanoparticles for the delivery of genes and drugs to human hepatocytes," <i>Nature Biology, Published online: 29 June 2003, doi:10.1038/nbt843</i> (August 2003 Volume 21 Number 8 pp 885-890) (2003)
*	Yan et al., "Membrane-anchored Aspartyl Protease with Alzheimer's Disease β-Secretase Activity," Nature 402:533-537 (1999)
*	Yang et al., "Hydrodynamic injection of viral DNA: A mouse model of acute hepatitis B virus infection," <i>PNAS</i> , 99, 21, 13825-13830 (2002)
*	Zamore et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell 101:25-33 (2000)
*	Ziche et al., "Angiogenesis Can Be Stimulated or Repressed <i>In Vivo</i> by a Change in GM3:GD3 Ganglioside Ratio," <i>Laboratory Investigation</i> 67:711-715 (1992)
*	Zinnen et al., "Chemically Modified siRNAa: Potential Anti-viral Hepatitis Therapeutics" (Abstract) March 2004

EXAMINER	DATE CONSIDERED